

REMARKS

The above amendments were made to place the claims into proper United States Patent Format.

Respectfully Submitted,



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1. A method of treating, preventing or ameliorating chronic heart failure or acute heart failure in a patient the method comprising administering to the patient an effective amount of a compound that is able to reduce the production, absorption and/or the effect of an endotoxin (lipopolysaccharide; LPS).

2. (amended) ~~A~~ The method of claim 1, wherein the heart failure includes treating, preventing or ameliorating endotoxin-mediated immune activation in acute or chronic heart failure in a patient the method comprising administering to the patient an effective amount of a compound that is able to reduce the production, absorption and/or the effect of an endotoxin (lipopolysaccharide; LPS).

3. (amended) A method according to claim 1 ~~and 2~~ wherein the compound is able to bind to an endotoxin (lipopolysaccharide; LPS) molecule.

4. (amended) A method according to claim 1 ~~to 3~~ wherein, the compound is able to reduce the available endotoxin in the patient.

5. (amended) A method according to claim 1 ~~to 4~~ wherein the compound is a bile acid.

6. (amended) A method according to claim 1 ~~to 5~~ wherein the bile acid is any one of ursodesoxycholic acid, chemodeoxycholic acid, dehydrocholic acid, cholic acid and deoxycholic acid.

7. (amended) A method according to claim 1 ~~to 6~~ wherein the compound is LPS binding protein, bactericidal/permeability increasing protein (BPI), a lipoprotein, for instance but not exclusively low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), apolipoprotein (a), a lipoprotein mixture or an antibody capable of binding to endotoxin (lipopolysaccharide; LPS).

8. (amended) A method according to claim 1 ~~and 2~~ wherein the compound is able to bind to an endotoxin (lipopolysaccharide; LPS) molecule in the gut.

9. (amended) A method according to claim 1, ~~2 and 8~~ wherein the compound is able to reduce the absorption of endotoxin by the patient from the gut.

10. (amended) A method according to claim 1, ~~2 and 8, 9~~ wherein the compound is able to substantially reduce tile availability of endotoxin (lipopolysaccharide) for absorption from the gut, such that the amount of endotoxin that is absorbed is reduced or is less biologically active.

11. (amended) A method according to claim 1, ~~2 and 8 to 10~~ wherein the compound is activated charcoal activated carbon, Fuller's earth, attapulgite, kaolin, bentonite or a clay or colostrum of human, bovine, or other mamallian origin

12. (amended) A method according to claim ~~1 and 2~~, wherein the compound is an antibacterial agent.

13. (amended) A method according to claim ~~1, 2 and 12~~ wherein the antibacterial agent is active in the gut.

14. (amended) A method according of claim ~~1, 2 and 12, 13~~ wherein the antibacterial agent is able to substantially reduce the amount of bacteria and/or free endotoxin (lipopolysaccharide) in the gut.

15. (amended) A method according of claim ~~1, 2 and 12 to 14~~ wherein the antibacterial agent is largely unabsorbed from the gut.

16. (amended) A method according of claim ~~1, 2 and 12 to 15~~ wherein the antibacterial agent is an antibiotic, for instance but not exclusively non-absorbable antibiotics like neomycin, tobramycin, amphotericin B, and colistin.

17. (amended) A method according to claim ~~1 and 2~~ wherein the compound is able to inhibit the response by a cell to endotoxin (lipopolysaccharide; LPS).

18. (amended) A method according to claim ~~1, 2 and 17~~
wherein the compound is able to decrease the cytokine production
by a cell in response to endotoxin (lipopolysaccharide; LPS).

19. (amended) A method according to claim ~~1, 2 and 17, 18~~
wherein the compound is an antibody able to bind the CD14
receptor, soluble CD14 receptor or an antibody or non-functional
agonist of a toll-like receptor, ~~particularly toll-like receptor~~
~~4 and 2~~.

20. (amended) A method according to claim ~~1, 2 and 17 to 19~~
wherein the compound is able to inhibit signalling via the CD14
receptor or via a toll-like receptor, ~~particularly toll-like~~
~~receptor 4 and 2~~.

21. (amended) A method according to claim ~~1 and 2~~
wherein the compound is able to reduce the permeability of
the gut wall to bacteria and/or endotoxin
(lipopolysaccharide; LPS).

22. (amended) A method according to claim ~~1, 2 and 21~~
wherein the agent is able to reduce the amount of bacteria
and/or free endotoxin (lipopolysaccharide) that is able to
translocate from the gut into the circulation of the patient.

23. (amended) A method according to claim ~~1, 2 and 21,~~
22 wherein the agent is largely unabsorbed from the gut.

24. (amended) A method according to claim ~~1, 2 and 21 to~~
23 wherein the agent is IGF-1, allopurinol, oxipurinol, or
any other unspecific xanthine oxidase inhibitor, or a
specific xanthine oxidase inhibitor (like TMX-67), liquorice
or its derivatives, ~~for example carbenoxolone,~~ an alginate,
sulfacrate or an agent that may form a hydrogel.

25. (amended) A method according to ~~any one of the~~
~~preceeding claims~~ claim 1 wherein the compound is administered
orally.

26. (amended) A method according to ~~any one of the~~
~~preceeding claims~~ claim 1 wherein the compound is
administered intravenously.

27. (amended) A method according to ~~any one of the~~
~~preceeding claims~~ claim 1 wherein the compound is
administered rectally.

~~28. Use of a compound that is able to bind to an endotoxin (lipopolysaccharide; LPS) molecule in the manufacture of a medicament for treating, preventing or ameliorating chronic heart failure or acute heart failure in a patient.~~

~~29. Use of a compound that is able to bind to an endotoxin (lipopolysaccharide; LPS) molecule in the manufacture of a medicament for treating, preventing or ameliorating endotoxin mediated immune activation in acute or chronic heart failure in a patient.~~

~~30. The use of claim 28 or claim 29 wherein the compound is a bile acid or LPS binding protein or bactericidal/permeability increasing protein (BPI), a lipoprotein, for instance but not exclusively low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), apolipoprotein (a), a lipoprotein mixture or an antibody capable of binding to endotoxin (lipopolysaccharide; LPS). or art antibody capable of binding to LPS.~~

~~31. Use of a compound that is able to bind to an endotoxin (lipopolysaccharide; LPS) molecule in the gut in~~

~~the manufacture of a medicament for treating, preventing or ameliorating chronic heart failure or acute heart failure in a patient.~~

~~32. Use of a compound that is able to bind to an endotoxin (lipopolysaccharide, LPS) molecule in the gut in the manufacture of a medicament for treating, preventing or ameliorating endotoxin mediated immune activation in acute or chronic heart failure in a patient.~~

~~33. The use of claim 31 or claim 32 wherein the compound is activated charcoal, activated carbon, Fuller's earth, attapulgite, kaolin or bentonite or a clay.~~

~~34. Use of an antibacterial agent in the manufacture of a medicament for treating, preventing or ameliorating chronic heart failure or acute heart failure in a patient.~~

~~35. Use of an antibacterial agent in the manufacture of a medicament for treating, preventing or ameliorating endotoxin mediated immune activation in acute or chronic heart failure in a patient.~~

~~36. The use of claim 34 or claim 35 wherein the compound is a non-absorbable antibiotic, for instance but not exclusively, like neomycin, tobramycin, amphotericin B, and colistin.~~

~~37. Use of a compound that is able to inhibit the response by a cell to endotoxin (lipopolysaccharide; LPS) in the manufacture of a medicament for treating, preventing or ameliorating chronic heart failure or acute heart failure in a patient.~~

~~38. Use of a compound that is able to inhibit the response by a cell to endotoxin (lipopolysaccharide; LPS) in the manufacture of a medicament for treating, preventing or ameliorating endotoxin-mediated immune activation in acute or chronic heart failure in a patient.~~

~~39. The use of claim 37 or claim 38 wherein the compound is an antibody able to bind the CD14 receptor, soluble CD14 receptor or an antibody or non-functional agonist of a toll like receptor, particularly toll like receptor 4 and 2..~~

40. ~~Use of an agent that is able to reduce the permeability of the gut wall to bacteria and/or endotoxin (LPS) in the manufacture of a medicament for treating, preventing or ameliorating chronic heart failure or acute heart failure in a patient.~~

41. ~~Use of an agent that is able to reduce the permeability of the gut wall to bacteria and/or endotoxin (LPS) in the manufacture of a medicament for treating, preventing or ameliorating endotoxin mediated immune activation in acute or chronic heart failure in a patient.~~

42. ~~The use of claim 40 or claim 41 wherein the agent is 1CF-1, allopurinol, oxipurinol, or any other unspecific xanthine oxidase inhibitor, or a specific xanthine oxidase inhibitor (like TMX-67), liquorice or its derivatives, for example carbenoxolone, an alginate, sulfaerate or an agent that may form a hydrogel.~~

43. (amended) ~~The method or use of any of the preceding~~ claims claim 1 ~~wherein a HMG-coenzyme A-reductase inhibitor that is able to increase lipoprotein levels and is not used to lower LDL / cholesterol levels is administered to the patient.~~

44. ~~The combined application of any method or use of any of the preceding claims in an individual patient.~~

45. (amended) ~~The method or use of any of the preceding~~
~~claims~~ claim 1 wherein a diuretic is administered to the
patient.

46. (amended) A pharmaceutical formulation according to
claim 78, wherein the compound is comprising bile acid or BPI
or LPS binding protein, a lipoprotein, ~~for instance but not~~
~~exclusively like low density lipoprotein (LDL), high density~~
~~lipoprotein (HDL), very low density lipoprotein (VLDL),~~
~~apolipoprotein (a),~~ a lipoprotein mixture, or an antibody
capable of binding LPS ~~and a diuretic.~~

47. (amended) ~~A~~ The pharmaceutical formulation according
to claim 78 comprising a compound that is able to bind to an
endotoxin (lipopolysaccharide; LPS) molecule in the gut and a
diuretic.

48. (amended) ~~A~~ The pharmaceutical formulation according
to claim 78 comprising an antibacterial agent and a diuretic.

49. (amended) ~~A~~-The pharmaceutical formulation according to claim 78 comprising a compound that is able to inhibit the response by a cell to endotoxin (lipopolysaccharide; LPS) and a diuretic.

50. (amended) ~~A~~-The pharmaceutical formulation according to claim 78 comprising an agent that is able to reduce the permeability of the gut wall to bacteria and/or endotoxin (LPS) and a diuretic.

~~51. Any novel method of treating, preventing or ameliorating acute or chronic heart failure as herein disclosed.~~

~~52. Any novel pharmaceutical composition as herein disclosed.~~

53. A method of treating or ameliorating body wasting or cachexia in a patient with liver cirrhosis, chronic obstructive pulmonary disease, chronic renal failure, diabetes, rheumatoid arthritis in a patient the method comprising administering to the patient an effective amount of a compound that is able to reduce the production,

absorption and/or the effect of an endotoxin
(lipopolysaccharide; LPS).

54. (amended) ~~A~~ The method of claim 53, wherein the
patient's condition further comprises ~~treating, preventing or~~
~~ameliorating endotoxin-mediated immune activation in body~~
~~wasting or cachexia in a patient with liver cirrhosis,~~
~~chronic obstructive pulmonary disease, chronic renal failure,~~
~~diabetes, rheumatoid arthritis the method comprising~~
~~administering to the patient an effective amount of a~~
~~compound that is able to reduce the~~ ¹⁵ ~~production, absorption~~
~~and/or the effect of an endotoxin (lipopolysaccharide; LPS).~~

55. (amended) ~~A~~ method according to claim 53 ~~and 54~~
wherein the compound is able to bind to an endotoxin
(lipopolysaccharide; LPS) molecule.

56. (amended) ~~A~~ method according to claim 53 ~~to 55~~
wherein the compound is able to reduce the available
endotoxin in the patient.

57. (amended) ~~A~~ method according to claim 53 ~~to 56~~
wherein the compound is a bile acid.

58. (amended) A method according to claim ~~53 to 56~~ 57 wherein the bile acid is any one of ursodesoxycholic acid, chemodeoxycholic acid, dehydrocholic acid, cholic acid and deoxycholic acid.

59. (amended) A method according to claim ~~53 to 56~~ wherein the compound is LPS binding protein.

60. (amended) A method according to claim ~~53 to 56~~ wherein the compound is bactericidal/permeability increasing protein (BPI).

61. (amended) A method according to claim ~~53 to 56~~ wherein the compound is, a lipoprotein, ~~for instance, low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), apolipoprotein (a), a lipoprotein mixture.~~

62. (amended) A method according to claim ~~53 to 56~~ wherein the ~~treatment~~ compound is a combination of a ~~compound according claim 59 and claim 61~~ LPS binding protein and a lipoprotein.

63. (amended) A method according to claim 53 ~~to 56~~
wherein the compound is ~~or~~ an antibody capable of binding to
endotoxin (lipopolysaccharide; LPS).

~~64. A method according to claim 53 to 56 wherein the
compound is or an antibody capable of binding to endotoxin
(lipopolysaccharide; LPS).~~

65. (amended) A method according to claim 53 ~~to 56~~ wherein
the compound is an antibody able to bind to the CD 14 receptor.

66. (amended) A method according to claim 53 ~~to 56~~
wherein the compound is a soluble CD14 receptor.

67. (amended) A method according to claim 53 ~~to 56~~
wherein the compound is a drug blocking effectively signaling
through toll-like receptors, ~~for instance toll like receptor
4 and toll like reeceptor 2.~~

68. (amended) A method according to claim 53 ~~to 56~~
wherein the compound is colostrum of human, bovine, or other
mamallian origin.

69. (amended) A method according to claim 53 ~~to 56~~
wherein the compound is able to inhibit the response by a
cell to endotoxin (lipopolysaccharide; LPS).

70. (amended) A method according to claim 53 ~~to 56 and 69~~
wherein the compound is able to decrease the cytokine
production by a cell in response to endotoxin
(lipopolysaccharide; LPS).

~~71. A method according to claim 53, 54 and 69, and 70
wherein the compound is a compound named in claim 57 to 68.~~

72. (amended) A method according to ~~any one of the~~
~~preceding claims~~ claim 53 wherein the compound is administered
orally.

73. (amended) A method according to ~~any one of the~~
~~preceding claims~~ claim 53 wherein the compound is
administered intravenously.

74. A method according to ~~any one of the preceding~~
~~claims~~ claim 53 wherein the compound is administered
rectally.

~~75. The combined application of any method or use of
any of the preceding claims in an individual patient.~~

76. (new) A method according to claim 17, wherein the
compound is an antibody able to bind the CD14 receptor,
soluble CD14 receptor or an antibody or non-functional
agonist against the toll-like receptor 4 and 2.

77. (new) A method according to claim 17, wherein the
compound is able to inhibit signalling via the CD14 receptor
or via the toll-like receptor 4 and 2.

78. (new) A pharmaceutical formulation comprising a
diuretic and a compound chosen from the group consisting of:

a) bile acid or BI or LPS binding protein, a
lipoprotein, a lipoprotein mixture, or an antibody capable
of binding LPS;

b) a compound that is able to bind to an endotoxin
(lipopolysaccharide; LPS) molecule in the gut;

c) an antibacterial agent;

d) a compound that is able to inhibit the response by
a cell to endotoxin (lipopolysaccharide; LPS); and

e) an agent that is able to reduce the permeability
of the gut wall to bacteria and/or endotoxin (LPS).

79. (new) A pharmaceutical formulation according to claim 78, wherein the compound is a lipoprotein chosen from the group consisting of low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), and apolipoprotein (a).

80. (new) A method according to claim 53, wherein the compound is a lipoprotein chosen from the group consisting of low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), apolipoprotein (a), a lipoprotein mixture.

81. (new) A method according to claim 53, wherein the compound is a drug blocking effectively signaling through the toll-like receptor 4 and toll-like receptor 2.